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CONTROL OF LABORATORY AIRBORNE INFECTION

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The control of laboratory airborne infection depends more on administrative and human factors than on the development of new procedures and equipment. The major problem is one of communication and conviction. Much more is known about control of potential airborne infection than is applied.

ADMINISTRATION

In microbiological units, safety against laboratory-acquired infection is not practiced fully because of lack of agreement on the danger by the administrators and lack of awareness by the workers. The analyses by Sulkin and Pike (36) show that only 16% of the illnesses in laboratory workers handling pathogenic microorganisms are due to definite accidents, whereas 65% or more of the cases may be caused by infectious aerosols (41). Laboratory directors are usually chosen for scientific and not for managerial ability with its rigorous respect for safety. The cardinal points of a safety program are education, engineering, and enforcement. Rules, standards, and operating procedures together with inspection, investigation, analysis, correction, and discipline are required as well as setting a good personal example. Oftentimes these directly oppose the philosophy of scientific freedom which comes with academic training.

One attitude which is a deterrent to safety is the martyr-to-science complex. "Have the disease and get it over with" is fortunately becoming less acceptable to younger personnel aware of potential permanent damage to health with its high cost and legalistic complications.

Technical information necessary to control laboratory airborne infection is not readily available. Much of it is lost in a maze of reports of limited circulation, mimeographed sheets of regulations and procedures, and tested practices not even written down.

To overcome these handicaps, education should be instituted to make protective practices part of every laboratory worker's activity. This must start with a firm unqualified statement of policy by the laboratory director, such as:

1) Planning for accident prevention will be part of all research, development, repair, and services.

2) No job will be considered so important that it cannot be done safely.

3) Each person is responsible for preventing accidents and infection during the course of his individual actions.

4) Each supervisor is responsible for:

a) Preventing accidents and infection during the course of work under his supervision to the same extent that he is responsible for any other part of his job.

b) Training persons under his supervision in safe working habits.

With clear policy, participation of employees is necessary to secure realistic regulations and group cooperation. A committee system is very useful in initiating a control program. Reports should be written, distributed to all persons in the laboratory including the highest administrative official, and all the work of this group should receive full recognition and encouragement for productivity.

Individual instruction of senior scientists in training their juniors is preferable to the less personal notices on the bulletin board, booklets, films, and departmental meetings. As DeReamer (7) has put it, laboratory "safety is contagious, and the best carrier of the contagion is the boss and the boss's boss."

The use of human engineering (21, 22) is desirable to improve safety by designing equipment in terms of human capabilities and limitations and to reduce resistance to change. The design should make it easy to act in a safe manner.

Infectious risk also may be reduced mechanically, allowing no alternative in method of accomplishing a hazardous operation as, for example, reducing or eliminating open laboratory bench-space at Fort Detrick. Other possible actions include:

1) Separate areas of unequal risk by designating "clean" and "contaminated" parts. Entry to the contaminated area should be through a

clothes-changing and shower room system. Communication without entry can be attained by use of electrical intercommunications systems, plastic speaking diaphragms, and glass viewing windows in doors and walls. Within the contaminated space, areas may be isolated from each other.

2) Regulate entrance to contaminated or infectious areas. Prohibit visitors and workmen unfamiliar with experiments.

3) Provide adequate autoclaves. Have separate autoclaves for sterilising contaminated articles from those for sterilization of bandages and instruments and have a separate area for holding infected animals.

4) Supply only needle-locking hypodermic syringes and only flat autoclavable pans for used pipettes and syringes.

5) Provide pipetting devices and prohibit mouth pipetting.

6) Provide only centrifuge trunnion cups with screw caps.

Microbiological Technique

The techniques needed to handle pathogenic organisms safely are so varied that it is not possible to do much more than refer to a few reviews on the subject (3, 20, 23, 32, 40). Some mention is now beginning to appear in textbooks (5, 25, 29). Unfortunately there is no single comprehensive evaluation of methodology. Undoubtedly some standard techniques may be hazardous only under some conditions with some organisms. Much could be learned during the course of experiments conducted primarily for other purposes by judicious sampling of air, surfaces, and personnel, and by use of uninoculated animal cage mates. During the housing of infected animals, airborne cross infection may affect the validity of the experiment (8). For instance, studies in our laboratories have shown that, during a test, cross infection of animals may be important in brucellosis (26) but, in the absence of aerosol challenge, is of no significance in vaccinia or Japanese B encephalitis. This permits caging requirements to be tailored to circumstances. Although many valuable incidental determinations of animal cross infection have been made, there are few instances of critical examination of the extent of its importance in the design of experiments. It is obvious that the demonstration of animal cross infection not only affects experimental validity but is indicative of some degree of human hazard.

Systematic investigation of hazards. The systematic investigation of the infectious hazards of laboratory procedures (28) offers many practical or developmental research problems suitable for training students in research methods. Diagnostic laboratories are in need of such studies, especially with regard to acquisition of tuberculosis by technicians (27). Some progress is being made in this connection (38, 45). Human autopsy practices are particularly vulnerable to examination (15, 31). Surprising results may emerge; for instance, the aerosols produced by a flush toilet have been studied recently by modern aerobiological techniques (6). Most interesting is that the mass median diameter of all bacterial-laden particles was 2.33 μ, with 9.5 bacteria per particle. These particles are well suited for inhalation. Their role in the epidemiology of such as yet unsolved diseases as infectious hepatitis must be considered.

The inherent hazard of a certain procedure sometimes is revealed when a highly virulent organism is used. *Pasteurella tularensis* is an excellent indicator of the adequacy of control measures. Infection of personnel will frequently occur with this bacterium when conventional methods of centrifuging are used and such common accidents as dropping petri dish cultures occur. Although some pessimism is justified in that few work long with *P. tularensis* without acquiring the disease, good technique plus suitable equipment can alter the picture.

A change in the growth medium may prove unexpectedly hazardous. The introduction of Tween (polyoxyethylene sorbitan monooleate)-broth, for growing *Mycobacterium tuberculosis hominis* in a dispersed state, is said to have been initially correlated with an increase in cases of tuberculosis in laboratories.

This discussion on techniques is directed at promoting more critical thought on safety by those who are at the laboratory bench. To reduce accidents and aerosols, the revisions in manipulations are usually so small and detailed that only the operator can think of them. For instance, a slight change in the position of the hands might result in reducing the number of self-inoculations with the hypodermic syringe. It would be interesting to see what changes would be made in microbiological tools, equipment, and manipula-

tive processes by the creative thinking of a man trained in tool design and uninhibited by the habitual thought of the microbiologist.

Engineering and Equipment

The engineering specifications and the equipment to control airborne infection depend upon a preceding analysis and definition of the problem. Application to a specific laboratory will vary significantly with the microorganisms in current use, degree of protection by vaccination, type of experiments, volume of infectious material, educational level of personnel, personalities, plans for the future, building structure, available or foreseeable equipment, finances, legal liability, and the extent to which political implications and public relations must be considered.

Critical thought on these questions will show that the steps taken to prevent airborne infection sometimes are those that are most convenient and obviously visible and not necessarily the most effective.

Clothing. Consider the traditional white clothing which in some aspects is similar to the witch doctor's headdress. There seems to be some magic protection connected with the wearing of white. Otherwise how can one excuse the entry of 30 persons into a surgical operating room or laboratory personnel in the lunch room or wards, wearing white gowns and white shoes seeded with assorted microorganisms? In this regard, the bacteriologist is falling below the standard he preaches to the surgeons (10). Clothing contaminated by obvious spills of pathogenic cultures should be autoclaved to prevent infection of laundry workers (24). Although the role of bacteria liberated from clothing has been studied in relation to its potential importance in hospitals (9), there seems to be no information on this subject about laboratories. Yet it is almost certain that, after some time, the laboratory gown and shoes of a technician working with tubercle bacilli at an open bench must harbor these organisms. With some vegetative pathogens, absence of specific disease suggests that microbiological shake-off from laboratory clothing is not significant. However, each laboratory should set up standards depending upon local conditions.

In a similar category is the gauze mask worn during hazardous laboratory operations. This mask has an average filtration efficiency of only 18%, when tested against inhaled bacteria containing droplet nuclei with a diameter of 1 to 5 μ (13). Dust respirators have a contrasting efficiency of more than 99%. Simple face masks, using a glass fiber filter with 90 to 95% efficiency, are now being developed by several commercial sources (1).

Air disinfection. Air disinfection and control are essential in preventing airborne infection. The basic physical principles underlying this subject have been elucidated by Wells (44). Briefly summarized, small infectious droplet nuclei with a diameter of less than 10 μ "... do not settle. Indoors they remain suspended until they are breathed or vented." Larger particles "... settle on everything indoors at an average velocity of 1 or 2 ft/min. Therefore, most of them settle before they are vented." High speed photography shows that many common laboratory techniques liberate both kinds of particles (16). These principles emphasize the importance of selective ventilation, ultraviolet radiation barriers, and other measures such as wet disinfectant cleaning instead of dry sweeping.

Direct ultraviolet irradiation of room air and room surfaces is useful in many situations in the laboratory (14, 42). Upper air irradiation is sufficiently less effective than downward directed irradiation, so it is not recommended for the usual laboratory although it may serve as a substitute for ventilation (23). An illustration of the potentiality of direct radiation may be seen from a hospital study which showed that the lamps had a disinfective effect with sprayed bacteria equivalent to 29 to 169 air changes per hour (17). Although ultraviolet lights are efficient when properly maintained, their pretty blue light still provides a sense of security long after the bactericidal effect is gone. Rarely is any methodical check made of their radiation. Often they are not kept clean. What is needed is an inexpensive survey meter, or an ultraviolet lamp that will change to an indicative color when it is no longer germicidal.

Exhaust air. Safety of exhaust air sometimes can be trusted to the dilution factor by discharge outside the building without treatment. The relation of the exhaust outlet to the building air intake and to open windows must be considered. A test with an odoriferous chemical will produce surprising results. But judgment must be exercised as is evident from a newspaper report of infection of nearby cattle by escape of the Afri

can type of foot-and-mouth disease virus in laboratory exhaust air (37). The usual medical diagnostic laboratory or the small infectious disease research unit needs nothing more than filtration or incineration of exhaust air at the point of origin of potential infective aerosol, commonly a ventilated cabinet, enclosure, inoculation room, or animal room.

For the larger installation there are now many excellent air purification devices of sufficient variety to meet any need. However, many institutions have engineering, maintenance, or custodial staffs who cannot keep these air systems in effective operation. Furthermore, failure to regulate the movement of people and materials and the inclusion of incompatible features such as laundry chutes and dumb waiters can negate the safety provided by a good air handling system. Consequently, we shall have an increasing number of expensive air handling systems that will remain impressively large and complicated but which slowly fail to fulfill their purpose. Filters will channel or be improperly seated so that air will by-pass the filters, or the filters will clog. Electrostatic devices and traveling oil curtains will short out or drop in effectiveness because of dust and sludge accumulation, and no one will be the wiser for some time. In this situation the maintenance force must be upgraded. Manufacturers need to give more attention to providing easily read indicators of the state of operating efficiency of their systems.

For instance, a pressure gauge is an excellent indicator of the condition of an air filter, but the usual air filter manufacturer leaves this detail up to the purchaser, who commonly does not realize when he needs such a gauge.

Use of positive air pressure in "clean" areas and negative air pressure in "contaminated" areas is a valuable concept, but control of air flow is difficult. Maintenance of air balance requires attention. An air system may start out all nicely balanced, but as soon as someone gets in the habit of having a door or window open at a critical point, the system is out of balance. A casual test with a lighted cigarette is not enough. Periodic use of smoke tubes, to see where the air is going, is recommended.

Air locks, change rooms, and personnel showers, especially if coupled with ultraviolet irradiation barriers and control of air flow, interrupt spread of airborne organisms (11, 33, 43).

Refuse. Cage litter from infected animals is a major problem. Its importance to the experiment and to the experimenter is incompletely known for many diseases. In the absence of this assessment for each animal, organism, route of injection, other variables in the experiment, bedding, and cage, it is sometimes best to use some form of ventilated cage or an ultraviolet barrier. In disposing of such litter, the animal caretaker is entitled to a knowledgeable judgment of its hazard and of precautions to be taken. These will vary. There may be germicidal wetting of the litter, pasteurization, or autoclaving before dumping into the trash can. Search for a dust-free litter is desirable. If human respiratory protection is to be used, the mask should provide more than token protection. Scrupulous cleanliness, 16 to 20 air changes an hour, and ultraviolet irradiation of the room may sometimes substitute for more elaborate caging. Refuse should be incinerated. The refuse transportation crew needs instruction and inspection of their handling practices, sometimes also vaccination and respirators. The National Institutes of Health are using an excellent trash can liner that simplifies this matter.

Sewage. Despite rules about pouring infected material into a sink, this does occur unless the laboratory is well controlled. Sometimes autoclaving is inadequate. There is one instance of Q fever being acquired by spectators during the cleaning of a blocked laboratory drain pipe (35). The most likely source was Lysol-soaked egg yolk material from Waring Blendors that was not autoclaved. Disinfection of laboratory sewage is not advised except in special circumstances involving large volumes of pathogenic culture, diseases in which sewage may have human epidemic potential, or organisms of unusual hazard, particularly those highly infectious for animals.

Control at point of origin. However, these measures do not get to the heart of the problem, namely, stopping the infectious aerosols at the point of origin. At this point the laboratory worker becomes personally involved. There are at least three major ways of protecting the worker. One is to externalize him by putting the infectious agent in a closed or semiclosed system of cabinets, animal cages, and other devices (12), not dissimilar from the methods used in studies with radioisotopes. The most important single item is the ventilated cabinet or hood from 3

to 6 ft long. Its use is also a good way to minimize the danger from those mishaps that accompany the inoculation of animals. Ingenious ventilated cabinets, animal cages, and centrifuge housings have been developed in England and Sweden to control laboratory-acquired tuberculosis (4, 18, 19, 46).

A second concept is that of internalizing the worker by providing a ventilated suit; or a ventilated head hood; or a gas mask, respirator, or other face mask in conjunction with protective clothing. Escape of infective amounts of agent into the room is then permissible. The room must be safeguarded under negative air pressure by an exhaust air filter and an ultraviolet air lock. A disinfectant shower may be provided for the ventilated suit. Peracetic acid (39) is recommended for such a shower. These arrangements are useful in handling monkeys and larger animals, which are difficult to control in cabinet systems when frequent examination is necessary, and in operating large experimental apparatus. The use of such rooms is facilitated by the suitability of β-propiolactone (2, 34) for disinfection of rooms and buildings and of ethylene oxide (30) for delicate instruments otherwise injured by autoclaving.

The third method is often the best. It combines a minimum of the other two methods, a maximum of personalized training in technique by the senior scientists, and specific immunization, when available. Recently we have experienced a striking example of this when substitution of a live tularemia vaccine for a killed vaccine resulted in elimination of cases of laboratory-acquired tularemia.

VACCINATION

Immunization, complete or partial, by infection or injection, has long been the substitute for attention to the training, technique, and equipment that will prevent illness. Few antigens artificially administered will protect the microbiologist against all accidental challenge. Botulinum, diphtheria, and tetanus toxoids, yellow fever vaccine, and probably smallpox vaccine are about all upon which certain reliance can be placed. Infection of vaccinated persons can be documented in other instances. Furthermore, the degree of immunity to aerosol challenge is unknown for some vaccines inasmuch as they have been standardized by other means.

Not only for the good of the laboratorian but from the long range view of national needs in times of peace and war, I wonder whether there might not be significantly greater benefit from more emphasis on development of vaccines rather than on engineering control of airborne laboratory infection. When I look at the papers in the immunological journals, I am puzzled by what seems to me a curious indifference to the real need for vaccines against brucellosis, psittacosis, Q fever, coccidioidomycosis, and the viral encephalitides, and for improved vaccines in the rickettsioses. In these diseases infection does produce some immunity, so it would seem that immunizing systems are present, awaiting development. Studies on the anthrax antigen, which show that part of an organism is a better immunogen that the whole dead organism, reveal what can be achieved by a new line of attack. The new poliomyelitis vaccines dramatize the potentiality of living vaccines. The comparatively greater emphasis upon research for curative drugs instead of for vaccines reflects man's age-old preference for cure of present need rather than for prevention of future possibility. Although we need education and engineering to control airborne laboratory infection, effective vaccines would be of more permanent value to the nation.

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